## REMARKS

The claims in the application are claims 1-5 and 7-12. New claim 12 is supported in the original specification at page 1, line 43, and the sequence listing at page 26 (renumbered as separate page 1).

Regarding the examiner's indication that the IDSs filed on March 20, 2001 and January 25, 2002 do not comply with 37 CFR 1.98(a)(3) is not understood, English equivalents are submitted herewith for each of the foreign language documents crossed through as not considered by the examiner:

WO 91/08229 = US 5,663,141;

EP 158 564 = US 5,705,355;

EP 346 616 = US 5,538,946 (previously filed);

DE 197 15 504 = WO 98/46648 (English language abstract on first page).

Entry and consideration of these references is requested. A PTO Form 1449 is attached. No fee should be required for this paper in view of the timely filed IDSs.

A replacement specification (including pages 1-41 which replace originally filed pages 1-25; the Abstract now as page 42; the sequence listing (as filed on August 10, 2001 by mail) as a separate page 1, as well as Figures 1-4) is attached. The replacement specification is double spaced, in accordance with 37 CFR § 1.52(b)(2)(i). The claims as filed are not included in the replacement specification since they are amended herein, which amendment contains a complete listing of all claims in the application double spaced.

Claims 4 and 5 have been rejected under 35 USC § 112, first paragraph, for lack of enablement. This rejection is respectfully traversed.

The Esslinger et al. article of record, in the summary and throughout, discloses PEG-hirudin of the half lives required by the instant claims. In particular, the values disclosed at page 916 amount to a terminal half life of 16 hours.

Claims 1-11 have been rejected under 35 USC § 112, second paragraph, for indefiniteness. This rejection is respectfully traversed.

All of the claims are now limited to PEG-hirudin. The claims are now clear that it is a prophylactic anticoagulant treatment that is being claimed and that an anticoagulant- effective amount of the PEG-hirudin is administered. The expression "at least" and the expression "about" are conventionally used in patent claims and are generally considered to be definite. See, e.g., *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1557, 220 USPQ 303, 316 (Fed. Cir. 1983). When, from the specification and the prior art, it may be considered that the meaning of the claims is in doubt, then the use of such terms might be considered indefinite. No such reasons are found in this case. See also MPEP § 2173.05(b)A.

The expression "enduring pharmacodynamic activity" is well known in this art and it is expressly defined in the present specification at page 5, lines 10-20. With respect to claim 6, the fact that mixtures of anticoagulant agents are comprehended is made clear at page 3, lines 1-4, of the specification. See also page 3 at lines 19-24 and 26-35.

There are no remaining multiple dependent claims, and it is believed that all ambiguities have been remedied by the claim amendments.

Claims 1-3 and 6-9 have been rejected under 35 USC § 102(b) as being anticipated by Bucha et al., DE 199 15 862 A1 (Bucha). This rejection is respectfully traversed.

The effective date of Bucha under 35 USC § 102(b) is its publication date of October 19, 2000. The effective date of the present application is March 20, 2000. Thus, Bucha is not a statutory reference.

Claims 1-3 have been rejected under 35 USC § 102(b) as being anticipated by DeRosa et al., US 5,723,576 (DeRosa). This rejection is respectfully traversed.

DeRosa relates only to hirudin *per se* and in no way suggests PEG-hirudin. Thus, it does not support a rejection for anticipation.

Claims 1-6 have been rejected under 35 USC § 103(a) as being unpatentable over Bucha in view of Bischoff, US 5,362,858. This rejection is respectfully traversed.

As demonstrated above, Bucha is not available as a reference. Thus, the combination can not establish obviousness.

Claims 1-11 have been rejected under 35 USC § 103(a) as being unpatentable over Bucha in view of DeRosa. This rejection is respectfully traversed since Bucha is not available as a reference.

In light of the foregoing amendments and remarks, it is respectfully submitted that all of the rejections have been obviated, and allowance of this application is

respectfully requested.

**A check in the amount of $930.00 is attached to cover the required three month extension fee.**

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,

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***MARKED-UP VERSION OF SPECIFICATION AMENDMENTS***

Attached is a replacement specification. The replacement specification includes pages 1-41 which replace originally filed pages 1-25; the Abstract now as page 42; the sequence listing (as filed on August 10, 2001 by mail) as a separate page 1, as well as Figures 1-4).

***MARKED UP VERSION OF CLAIM AMENDMENTS***

1. (currently amended) A method for the prophylactic anticoagulant treatment of a subject whose blood has undergone extracorporeal circulation, wherein an anticoagulant effective amount of ~~an anticoagulant agent~~ PEG(polyethylene glycol)-hirudin is administered to said subject.

3. (currently amended) The method of claim 1 ~~A method for treating a subject with extracorporeal circulation,~~ wherein an effective amount of ~~an anticoagulant agent~~ PEG-hirudin is administered to said subject for effective anticoagulant protection during the extracorporeal circulation and for prophylaxis of vascular complications after the extracorporeal circulation.

5. (currently amended) A method as claimed in claim 4, wherein the anticoagulant agent has an enduring anticoagulant pharmacodynamic activity.

Cancel claim 6.

8. (currently amended) A method as claimed in claim 7, wherein ~~the anticoagulant agent~~ PEG-hirudin is administered in the form of a single dose per hemodialysis.

10. (currently amended) A method as claimed in claim 8, wherein the amount of the single dose administered for a hemodialysis is such that the ~~APTT~~ activated thromboplastic time (APTT) is prolonged about 2.7-fold to about 1.8-fold during the hemodialysis.

12. (new) The method of claim 1 in which the PEG-hirudin is derived from recombinant hirudin.

***COMPLETE LISTING OF ALL CLAIMS IN THE APPLICATION***

1. (currently amended) A method for the prophylactic anticoagulant treatment of a subject whose blood has undergone extracorporeal circulation, wherein an anticoagulant effective amount of PEG(polyethylene glycol)-hirudin is administered to said subject.

2. (original) A method as claimed in claim 1, for the prophylaxis of vascular complications after the extracorporeal circulation.

3. (currently amended) The method of claim 1 wherein an effective amount of PEG-hirudin is administered to said subject for effective anticoagulant protection during the extracorporeal circulation and for prophylaxis of vascular complications after the extracorporeal circulation.

4. (previously amended) A method as claimed in claim 1, wherein the anticoagulant agent has a terminal half-life of at least about 4 hours.

5. (currently amended) A method as claimed in claim 4, wherein the anticoagulant agent has an enduring anticoagulant pharmacodynamic activity.

6. (canceled).

7. (previously amended) A method as claimed in claim 1, for treating a subject with chronic renal insufficiency requiring regular hemodialysis.

8. (currently amended) A method as claimed in claim 7, wherein PEG-hirudin is administered in the form of a single dose per hemodialysis.

9. (original) A method as claimed in claim 8, wherein the single dose is administered at

the start of a hemodialysis.

10. (currently amended) A method as claimed in claim 8, wherein the amount of the single dose administered for a hemodialysis is such that the activated thromboplastic time (APTT) is prolonged about 2.7-fold to about 1.8-fold during the hemodialysis.

11. (previously amended) A method as claimed in claim 8, wherein the amount of the single dose administered for a hemodialysis is such that the APTT is prolonged at least about 1.2-fold until the next hemodialysis.

12. (new) The method of claim 1 in which the PEG-hirudin is derived from recombinant hirudin.